Tumours of the Retina

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CONTENT

- Definition
- Etiology
- Genetics
- Pathology
- Clinical course
- Classification
- Diagnosis
- Treatment

Classification

1. Primary tumours

2. Secondary tumours

Retinoblastoma

- It is a common malignant tumour arising from the neurosensory retina.

- It is a proliferation of neural cells which have failed to evolve normally.

Aetiology

1. Prevalence: Most common intraocular tumour of childhood occurring 1 in 20,000 live birth.
2. Age: Confined to infancy and very young children.
3. Sex: No sex predisposition
4. Race: Rarer in Negroes than Whites
5. Bilaterality: In 25-30% b/l involvement, one eye is affected more extensively and earlier than the other.

Genetics

- First cancer to be directly associated with genetic abnormality
- Deletion or mutation of the q14 band of chromosome 13.
- This chromosome responsible for controlling retinal cell division.

Pathology

- Growth consists of small round cells with large nuclei resembling the cells of the nuclear layers of the retina.
- Many of these stain poorly, showing that they are undergoing necrosis.
- When noticed very early, a larger mass is seen surrounded by numerous punctuate satellites.
- Microscopically, minute deposits are seen scattered in various areas throughout the globe.

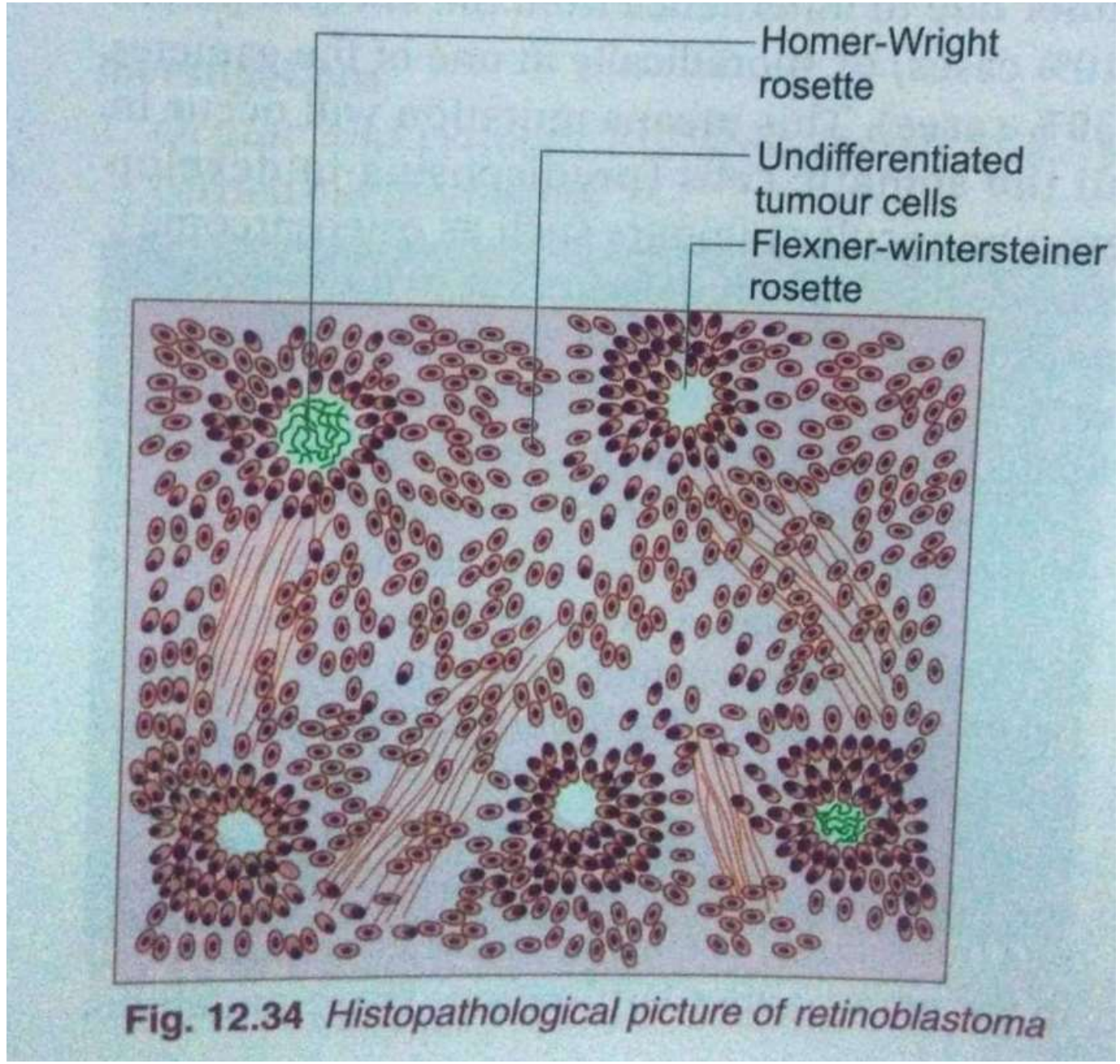


Fig. 12.34 *Histopathological picture of retinoblastoma*

- It may grow mainly outwards, separating the retina from the choroid --glioma exophytum
- inwards towards the vitreous -glioma endophytum

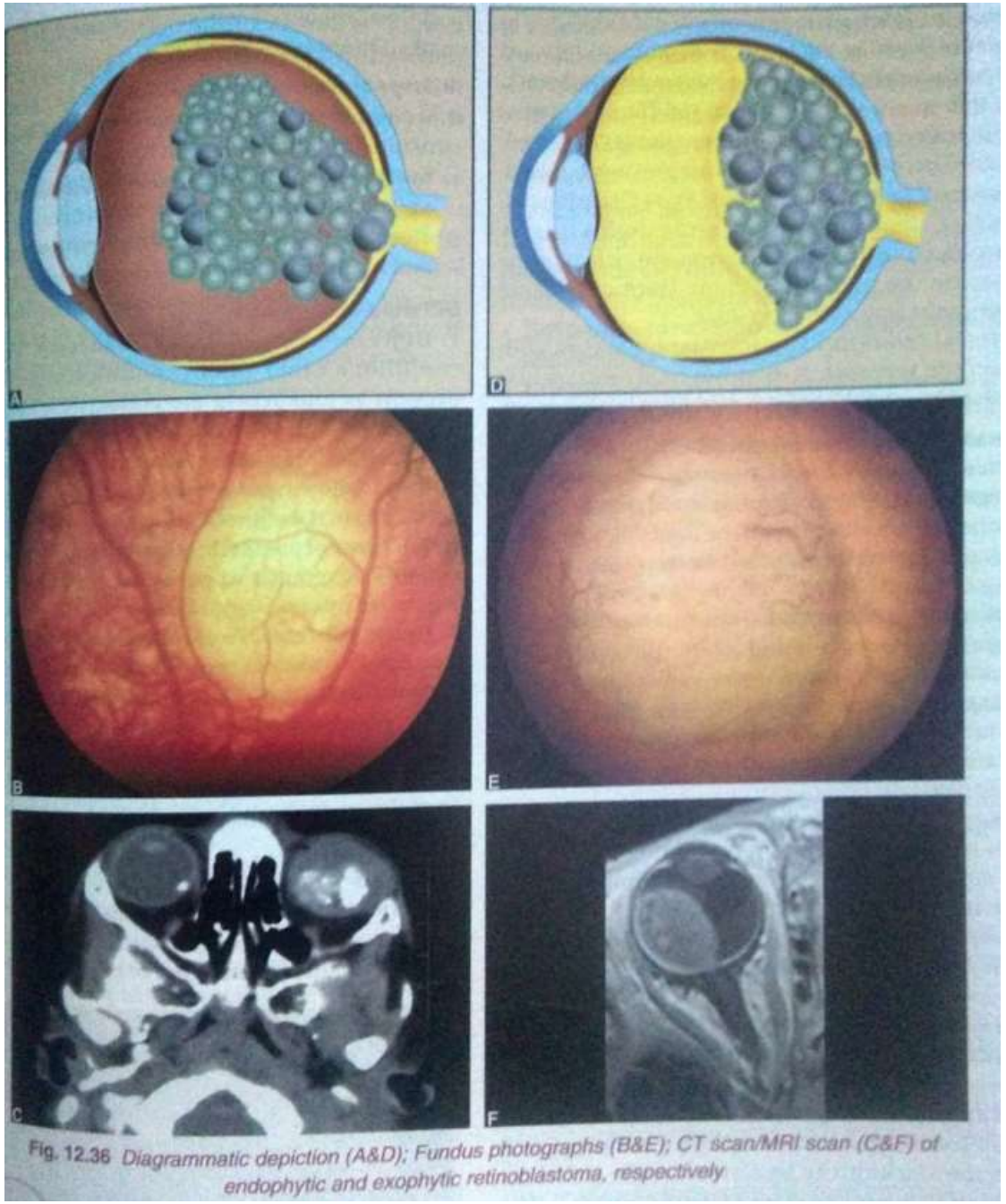


Fig. 12.36 Diagrammatic depiction (A&D); Fundus photographs (B&E); CT scan/MRI scan (C&F) of endophytic and exophytic retinoblastoma, respectively

Clinical course

- The child is usually brought to the hospital on account of a peculiar yellow- white reflex from the pupil, sometimes called leukocoria or ‘amaurotic cat’s eye’.
- Other modes of presentation include –
- convergent or divergent squint
- Buphthalmos
- Hypopyon or proptosis.

Fig. 12.35 *Leukocoria right eye in a patient with retinoblastoma*

- If left untreated retinoblastoma runs through the same stages as melanoma of the choroid:

1. The quiescent stage, lasting from 6 months to a year
2. The glaucomatous stage
3. The stage of extraocular extension
4. The stage of metastasis.

- The second stage results in enlargement of the globe with severe pain.
- Relieved when tumour bursts through the sclera, usually occurs at the limbus and followed by rapid fungation.

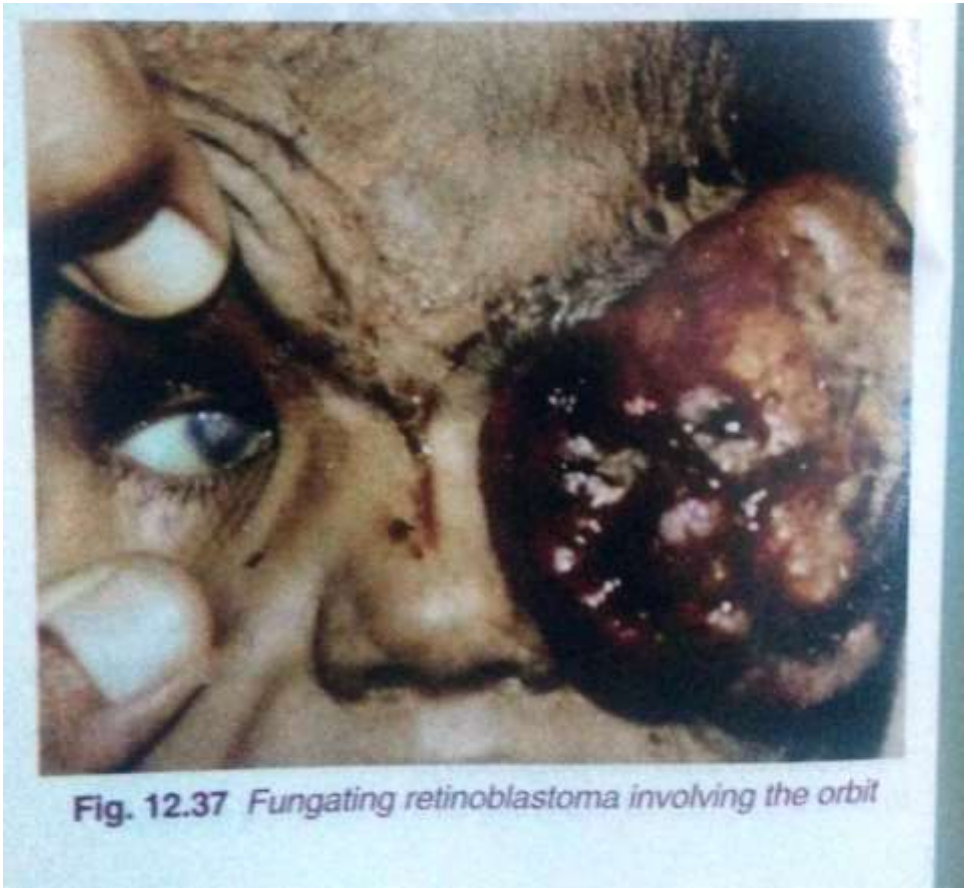


Fig. 12.37 *Fungating retinoblastoma involving the orbit*

- Metastasis first occurs in the preauricular and neighbouring lymph nodes, later in the cranial and other bones.
- Direct extension by continuity to the optic nerve (which is affected early) and brain is more common, while metastases in other organs, usually the liver, are relatively rare.
- Clinically a cauliflower-like mass arising from the retina is seen extending into the vitreous (exophytic type).

- There is neovascularization on the surface with white areas of calcification.
- Vitreous or anterior chamber seedings are seen as fluffy whitish-grey deposits.
- The endophytic type of retinoblastoma presents as an exudative retinal detachment, the summit of which is immobile.
- Secondary glaucoma is common, hypopyon with esotropia is sometimes the presenting clinical picture.

Classification

1. Reese and Ellsworth classification : which was of prognostic significance for the control of local disease.

- Most patients were treated by either enucleation (removal of the eye) or local therapies such as external beam radiation therapy and cryotherapy.
- This classification was used to predict which eyes were likely to survive local therapy and keep useful vision.

Group I. Very favourable for maintenance of sight:

- Solitary tumour, smaller than 4 DD in size, at or behind the equator
- Multiple tumours, none larger than 4 DD in size, all at or behind the equator.

Group II. Favourable for maintenance of sight:

- Solitary tumour, 4–10 DD in size, at or behind the equator
- Multiple tumours, 4–10 DD in size, behind the equator.

Group III. Possible to maintain sight:

- Any lesion anterior to the equator
- Solitary tumour, larger than 10 DD in size, behind the equator.

Group IV. Unfavourable for maintenance of sight:

- Multiple tumours, some larger than 10 DD in size
- Any lesion extending anteriorly to the ora serrata.

Group V. Highly unfavourable for maintenance of sight:

- Massive tumours involving more than one half the retina
- Vitreous seeding.

- Improved diagnostic techniques, including the indirect ophthalmoscope and new treatment options, underline the need for a revision of the Reese–Ellsworth classification.

2. International Classification:

- The prognosis for 5-year disease-free survival in intraocular retinoblastoma is more than 90%.
- In extraocular extensions the 5-year disease-free survival is less than 10%.
- The International Classification of Retinoblastoma was devised in 1990, to reflect changing paradigms in therapy, with chemotherapy becoming the treatment of choice.

TABLE 23.1 International Classification of Retinoblastoma

Group	Quick Reference	Specific Features
A	Small tumour	Rb < 3mm*
B	Larger tumour Macula Juxtapapillary Subretinal fluid	Rb > 3 mm* or Macular Rb location (< 3mm to foveola) Juxtapapillary Rb location (< 1.5 mm to disc) Subretinal fluid < 3 mm from margin
C	Focal seeds	Rb with Subretinal seeds < 3 mm from Rb Vitreous seeds < 3 mm from Rb Both subretinal and vitreous seeds < 3 mm from Rb
D	Diffuse seeds	Rb with Subretinal seeds > 3 mm from Rb Vitreous seeds >3 mm from Rb Both subretinal and vitreous seeds > 3 mm from Rb
E	Extensive Rb	Massive Rb with anatomic or functional destruction of the eye and/or Neovascular glaucoma Opaque media from haemorrhage in anterior chamber, vitreous or subretinal space Invasion of post-laminar optic nerve, choroid (>2 mm), sclera, orbit, anterior chamber Tumour touching lens Diffuse infiltrating tumour Phthisis or pre-phthisis

Rb—retinoblastoma; *refers to 3 mm in basal dimension or thickness

Differential Diagnosis

- Several conditions occurring in children may give rise to similar signs, and cause great difficulty in diagnosis
- These have been grouped together under the term pseudoglioma.

- The chief ones are:

(i) Inflammatory deposits in the vitreous, with or without detachment of the retina following a plastic cyclitis or choroiditis

(ii) Congenital defects such as Norrie disease and persistent hyper-plastic vitreous at the back of the lens

(iii) Retrolental fibroplasia

Diagnosis

- Calcification occurs in 75% of cases.
- X-rays can demonstrate calcification within the tumour
- Computerized tomography scan is more sensitive, as it also delineates the tumour and extension.
- Ultrasonography

- B-scan ultrasonography displays a cauliflower-like mass arising from the retina, with or without a retinal detachment, or vitreous seedings.
- A scan through the mass shows a characteristic V–Y pattern, as the tumour tissue is echo dense giving rise to high spikes and areas of necrosis within the mass return spikes of lower amplitude.

- Biochemical tests are rarely helpful.
- If the lactic dehydrogenase (LDH) activity is raised in the aqueous relative to the serum level, it is suggestive of retinoblastoma.

Treatment

- Small tumour by local modalities such as cryotherapy for anterior lesions
- Photocoagulation for posterior ones
- Brachytherapy with 60Co or 125I can be used.

- Radioactive cobalt discs sutured to the sclera over the site of the nodule are employed to deliver a dose of 4000 rad to the summit of the tumour in 1 week.
- The isotope 125I is increasingly being used and the plaques are custom-built for each child.
- Late sequelae of irradiation are thin greyish exudates at the macula appearing 18 months after treatment, and posterior cortical lens opacities becoming evident after a varying period (9 months to 8 years).

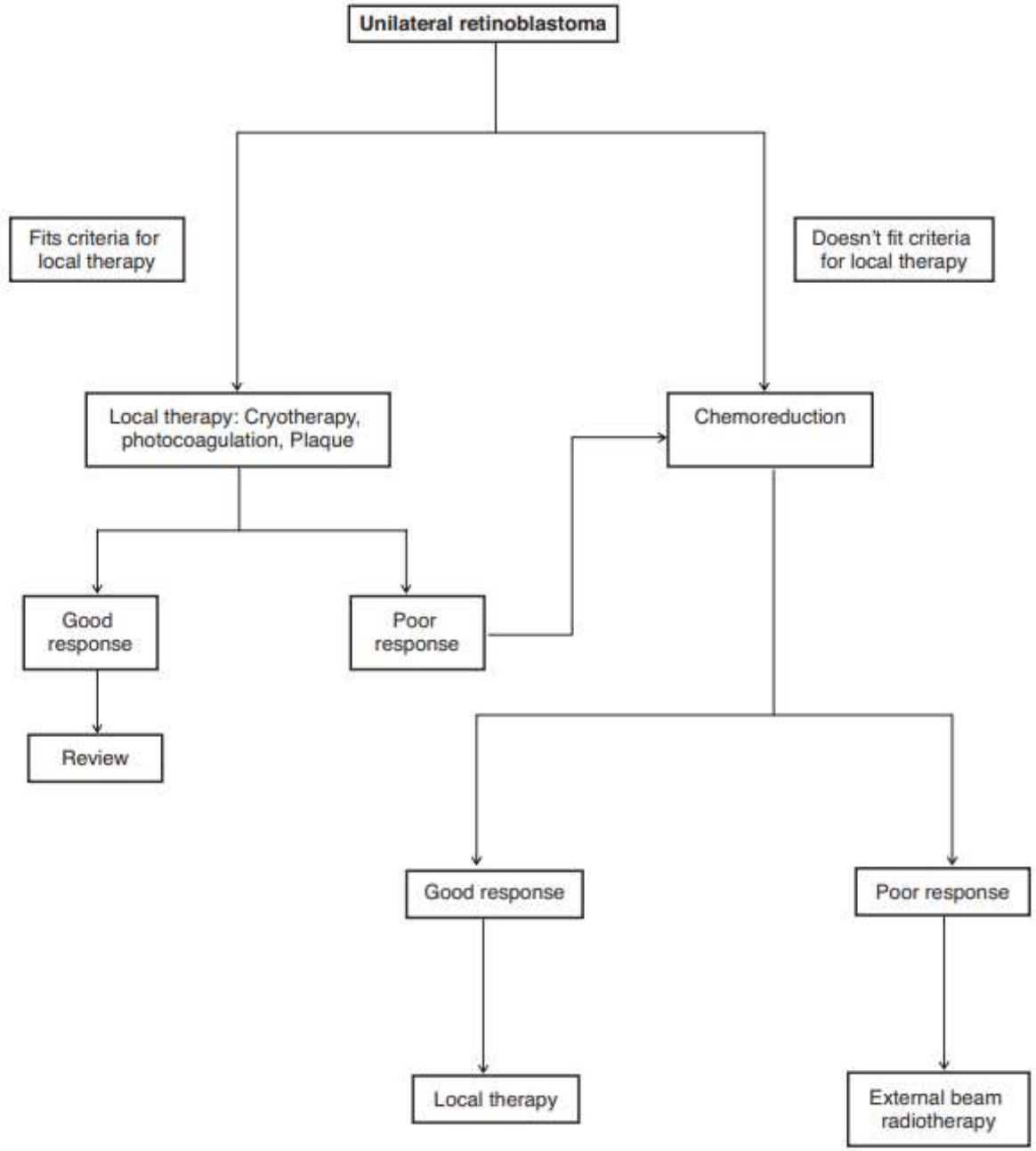
- In chemoreduction, combinations of chemotherapy are used to shrink the tumour, then therapy as for smaller tumours.
- The chemotherapy agents commonly used are a 3-drug combination of vincristine (typically 0.05 mg/kg for children 36 months or younger and 1.5 mg/m2 for older children), carboplatin (18.6 mg/kg for children 36 months or younger and 560 to 600 mg/m2 for older children), and etoposide (5 mg/kg for children 36 months or younger and 150 mg/m2 for older children).

- Multimodality, sequential local therapies such as laser therapy, cryotherapy and local ‘plaque’ radiotherapy are then used, as they have not been shown to produce secondary malignancies.
- Treatment for large tumours have now increased, with chemoreduction being done prior to an attempt at local management or enucleation.
- During enucleation, the optic nerve has to be cut at least 10 mm from the globe, and the cut end submitted to microscopic examination.

- Extension of the disease to the conjunctiva or orbital tissues warrant exenteration of the orbit.
- External beam radiation therapy was an alternative to enucleation.
- However, an increasing number of children who were give radiation before they were 1 year of age have been found to develop secondary malignancies (particularly within the irradiated field).

- The prognosis of retinoblastoma, if untreated, is always bad, and the patient invariably dies.
- Success with chemoreduction for retinoblastoma, defined as avoidance of external-beam radiation and enucleation-
- 100% for group A
- 93% for group B
- 90% for group C
- 47% for group D in the International Classification.

- In the absence of disease of the fellow eye the patient may be regarded as out of danger, if there is no recurrence in the orbit within 3 years, but the remaining eye should be carefully examined under dilatation at frequent intervals for a much longer period.
- Owing to its familial tendency the eyes of subsequent siblings or descendants should be carefully watched during infancy and childhood.


Unilateral retinoblastoma
Fits criteria for local therapy
Doesn't fit criteria for local therapy
Local therapy: Cryotherapy, photocoagulation, Plaque
Chemoreduction
Good response
Poor response
Review
Good response
Poor response
Local therapy
External beam radiotherapy

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